Surgical Management of High Risk Prostate Cancer

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Radical Prostatectomy for High Risk

High Risk Prostate Cancer: the Best Indication for Radical Prostatectomy

Dr. Hendrik Van Poppel
Leuven, Belgium

The optimal management of high risk prostate cancer (PCA) is a tremendous challenge for urologists and oncologists. Radiotherapy (RT) and radical prostatectomy (RP) are currently the radical treatment options for high risk PCA. Surgery for high risk PCA is gaining popularity since 10-year cancer specific survival (CSS) rates of more than 90% have been described.

The exact definition of high risk PCA remains an issue of debate. For example, D’Amico et al define high risk localized PCA as prostate specific antigen (PSA) 20 ng/ml or greater, or biopsy Gleason score (GS) 8-10, Translational Research) study group recently published a nomogram predicting specimen confined PCA (pT2-pT3a N0, negative surgical margins).2 Of the 1,366 patients with high risk PCA who underwent RP 37% had specimen confined disease at final pathology. These patients had an excellent 10-year CSS of 98.2% vs 87.6% for those with non-specimen confined PCA (p <0.001).

Another important aspect is tumor downgrading at the time of surgery. Several studies conclude that approximately a third of patients with a biopsy GS of 8 have disease downgraded to GS 7 or less in the RP specimen and had a better outcome. A recent study comparing RP with RT plus hormonal therapy (HT) for high risk prostate cancer in patients with biochemical progression found no significant difference in CSS.

There is only retrospective evidence from high volume centers and these studies show high rates of multimodal treatments. In recent years there has been a shift toward modern treatment approaches such as high dose RT, improved delivery of external beam and interstitial RT, and more extensive pelvic lymph node dissection (PLND). There is clear evidence that external beam radiotherapy (EBRT) combined with neoadjuvant and adjuvant androgen deprivation therapy (ADT) is superior to RT alone. Whether all patients should be on long-term ADT and for how long are still debated.

...a multimodal approach for high risk PCA is key, but surgery offers the possibility of tailoring eventual adjuvant or salvage treatment measures.

RP can be considered a valid strategy as the only therapy or the initial step of multimodal treatment with good OS and excellent CSS rates. One of the reasons to opt for RP is that at least 20% of patients do not have adverse pathology and will obtain the greatest benefit from surgery alone. RP performed by experienced surgeons in the modern era is associated with minimal treatment related morbidity due to advances in surgical technique, extended lymphadenectomy, decreased anesthesiologic risk and better perioperative management. The improved surgical technique minimizes incontinence and impotence. By choosing RP we avoid early and late RT toxicity and secondary cancers.

RP is the only treatment that provides definitive histopathological information as well as optimal locoregional control. Moreover, RP obviates the need for HT or allows its postponement. The optimal treatment of high risk PCA includes surgery as the initial step as patient
Radical Prostatectomy/High Risk

• Modern Radical Prostatectomy/ “Not your Father’s Radical Prostatectomy”
• Must be incorporated into a multi-Disciplinary multi-modality Rx plan
• Patient selection/practical issues
• Open vs. Robotic?
Radical Prostatectomy/High Risk

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Modern Radical Prostatectomy/ “Not your Father’s Radical Prostatectomy”

- In 2017, a modern radical prostatectomy can be performed with limited peri-operative morbidity
- Low transfusion rates: 1-10%
- Short hospitalization: 1-2 days.
- Low risk of long term incontinence: 2-10%
- Impotence risk is an issue/appropriateness of nerve-sparing technique in high risk questioned
- Your Father’s “high risk case” may not be the same today
Over Half of Contemporary Clinical Gleason 8 on Prostate Biopsy are Downgraded at Prostatectomy

• **Introduction:**
  • Accurate biopsy Gleason scoring is critical for the proper risk-stratification and treatment of prostate cancer.
  • Clinical Gleason ≥ 8 stratifies patient into “high-risk” category
  • There is an alarming discrepancy between prostate cancer diagnosed as Gleason 8 on biopsy and their actual pathology after radical prostatectomy.

• **Patients & Methods:**
  • Single-surgeon series (JWM) of 1034 men who underwent open RP between 2004 and 2015
  • 112 men (10.8%) had clinical Gleason 8
    • 9 patients excluded
      • 5 aborted surgery, 4 lacked surgical pathology scoring
Over Half of Contemporary Clinical Gleason 8 on Prostate Biopsy are Downgraded at Prostatectomy

• Results:
  • 61.1% (63/103) downgraded
  • 84.2% (32/38) downgraded 2012-2015

• Conclusions:
  • High-risk prostate cancer may be greatly overdiagnosed
  • Patients are at great risk of overtreatment and distress
  • Refining prostate cancer diagnostic techniques should focus on high-risk clinical diagnoses as well

Downgrade associated with:
• lower PSA at biopsy
• decreased tumor percentage
• decreased likelihood of positive margins
Duke RRP Moul 2004-2015 Risk-Stratification by Year
Gleason Score by Year
Increase in Higher Risk PCa Following New USPSTF Screening Recommendations

Percentage of Patients with PSA > 10 ng/mL

PSA > 10, All Men

PSA > 10, Age > 74

Y-axis range < 100%

Hall MD, et al. Increase in higher risk prostate cancer cases following new screening recommendation by the US Preventive Services Task Force (USPSTF). Poster presented at: Annual Meeting of the American Society of Clinical Oncology; May 29-June 2, 2015; Chicago, IL. Abstract 143.
Radical Prostatectomy/High Risk

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Utilization Trends at a Multidisciplinary Prostate Cancer Clinic: Initial 5-Year Experience From the Duke Prostate Center


From the Division of Urology (SBS, LLB, CNR, SJF, TJP, DX, JWM) and Duke Prostate Center, Department of Surgery (SBS, LLB, CNR, SJF, TJP, DX, JWM), Departments of Pathology (SJF) and Radiation Oncology (BFR, ZV, WRL) and Division of Medical Oncology, Department of Medicine (AJA, PGF, DJG), Duke University Medical Center and Department of Surgery, Durham Veterans Affairs Medical Center (SJF), Durham, North Carolina

Purpose: The multidisciplinary approach is becoming increasingly encouraged but little is known about the multidisciplinary experience compared to routine care. For patients with prostate cancer the goal is to provide evaluations by urologists, medical and radiation oncologists at a single visit. Although additional resources are required, this strategy may enhance the overall health care experience. We compared utilization determinants between a multidisciplinary and a urology prostate cancer clinic at Duke University Medical Center and identified factors associated with pursuing treatment at the university medical center for multidisciplinary clinic patients.

Materials and Methods: We retrospectively analyzed data on patients referred for primary prostate cancer treatment evaluation at Duke University Medical Center from 2005 to 2009. Comparisons between 701 multidisciplinary clinic and 1,318 urology prostate cancer clinic patients were examined with the rank sum and chi-square tests. Predictive factors for pursuing treatment at the university medical center were assessed using multivariate adjusted logistic regression.

Results: Compared to patients at the urology prostate cancer clinic those at the multidisciplinary clinic were more likely to be younger and white, have a higher income and travel a longer distance for evaluation. Of multidisciplinary clinic patients 58% pursued primary treatment at the university medical center. They were more likely to be younger, black and physician referred, have a lower income and reside closer to the medical center. Factors predictive of pursuing treatment at the medical center included high risk disease and physician referral. Factors predictive of not receiving care at the university medical center were income greater than $40,000 and a distance traveled of greater than 100 miles.

Conclusions: A different patient demographic is using the multidisciplinary approach. However, when treatment is pursued at the institution providing multidisciplinary services, the patient demographic resembles that of the treating institution.

Abbreviations and Acronyms
BMI = body mass index
CAPRA = Cancer of the Prostate Risk Assessment
DUMC = Duke University Medical Center
MDC = multidisciplinary clinic
PC = prostate cancer
UPCC = urology prostate cancer clinic

Submitted for publication May 6, 2011. Study received Duke University Medical Center institutional review board approval.
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† Financial interest and/or other relationship with Lipid Management Ltd., Astellas, Sanofi-Aventis, AstraZeneca, GlaxoSmithKline and Farma.
‡ Financial interest and/or other relationship with Sanofi-Aventis, AstraZeneca, GlaxoSmithKline and Farma.
§ Financial interest and/or other relationship with Sanofi-Aventis, AstraZeneca, GlaxoSmithKline and Farma.

Ref: Stewart SB, Banez LL, Robertson CN…Moul JW et al. J Urol. JAN 2012 issue
Baseline Characteristics of Duke Multi-D Patients: One-Third High Risk

D'Amico et al. Risk Stratification

- Low: 45.4%
- Intermediate: 21.5%
- High: 33.1%

1D’Amico AV. JAMA. 1998; 280
## Multi-D Clinic: Predictors of Pursuing Treatment at Duke

<table>
<thead>
<tr>
<th>Duke Treatment Predictor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>1.12</td>
<td>0.52—2.43</td>
<td>0.770</td>
</tr>
<tr>
<td>BMI</td>
<td>2.09</td>
<td>0.50—8.70</td>
<td>0.307</td>
</tr>
<tr>
<td>CAPRA 6-10 (High Risk)</td>
<td>2.52</td>
<td>1.23—5.19</td>
<td>0.012</td>
</tr>
<tr>
<td>Clinic year</td>
<td>0.96</td>
<td>0.83—1.12</td>
<td>0.642</td>
</tr>
<tr>
<td>Income</td>
<td>1.06</td>
<td>0.49—1.93</td>
<td>0.873</td>
</tr>
<tr>
<td>Distance &gt;100 mi</td>
<td>0.36</td>
<td>0.19—0.68</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Patients with a **CAPRA score 6-10 (HIGH RISK)** were **2.5x more likely to pursue** treatment at Duke.
Must be incorporated into a multi-Disciplinary multi-modality Rx plan

- Radical prostatectomy for high risk patients should generally not be planned in a vacuum.
- Discussion in the context of a multi-disciplinary team before the operation is ideal
- Clinical trial opportunities should be encouraged
RP + Neoadjuvant Chemotherapy

- Positive trials in CRPC & M1 with taxanes
  - SWOG 9916; TAX 327; CHARRTED
- Pilot studies on neoadjuvant chemotherapy generally safe
- Phase III trial completed enrollment in 2015
  - CALGB 90203 (PUNCH)
- Not standard of care as of 2017

CALGB 90203: Phase III Study of Radical Prostatectomy Alone +/- Docetaxel in High-Risk Localized Prostate Cancer (PUNCH)

- High-risk localized CAP
- RANDOMIZE
- RP
- Primary EPC = 5-year bPFS
- ADT + docetaxel followed by RP

Phase III Study of Adj. Chemotherapy in Post-RP High-Risk Prostate Cancer: SWOG 9921

STATUS POST RADICAL PROSTATECTOMY (T3b, T4, or N1, GS ≥ 8, T3a + margin, and GS 7)

N = 1,360 (to detect a 30% survival difference)

RANDOMIZE

CAB x 24 months

Mitoxantrone changed to docetaxel + prednisone 5 mg (bid) every 3 weeks x 6 and CAB x 24 months

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Patient selection/practical issues: Ideal Candidates?

- All D’Amico et al High Risk?
- Clinical T3/4?
- Only “young” men?
- *What combination of risk, age, health, and patient desire go into selection equation?*
Risk-Adapted Staging: D’Amico et al Risk Stratification

LOW RISK  PSA < 10 ng/ml and
Biopsy Gleason <= 6 and
1992 AJCC T_{1c, 2a}

INT RISK  PSA > 10 - 20 ng/ml or
Biopsy Gleason 7 or
1992 AJCC T_{2b}

HIGH RISK PSA > 20 ng/ml or
Biopsy Gleason \geq 8
1992 AJCC T_{2c}
Cancer-Specific Mortality After Surgery or Radiation for Patients With Clinically Localized Prostate Cancer Managed During the Prostate-Specific Antigen Era

By Anthony V. D’Amico, Judd Moul, Peter R. Carroll, Leon Sun, Deborah Lubeck, and Ming-Hui Chen

Purpose: To determine whether pretreatment risk groups shown to predict time to prostate cancer-specific mortality (PCSM) after treatment at a single institution retained that ability in a multi-institutional setting.

Patients and Methods: From 1988 to 2002, 7,316 patients treated in the United States at 44 institutions with either surgery (n = 4,946) or radiation (n = 2,370) for clinical stage T1c-2, N0 or NX, M0 prostate cancer made up the study cohort. A Cox regression analysis was performed to determine the ability of pretreatment risk groups to predict time to PCSM after treatment. The relative risk (RR) of PCSM and 95% confidence intervals (CIs) were calculated for the intermediate- and high-risk groups relative to the low-risk group.

Results: Estimates of non-PCSM 8 years after prostate-specific antigen (PSA) failure were 4% v 15% (surgery versus radiation; \( P_{\log \text{rank}} = .002 \)) compared with 13% v 18% (surgery versus radiation; \( P_{\log \text{rank}} = .35 \)) for patients whose age at the time of PSA failure was less than 70 as compared with \( \geq 70 \) years, respectively. The RR of PCSM after treatment for surgery-managed patients with high- or intermediate-risk disease was 14.2 (95% CI, 5.0 to 23.4; \( P_{\text{Cox}} < .0001 \)) and 4.9 (95% CI, 1.7 to 8.1; \( P_{\text{Cox}} = .0037 \)), respectively. These values were 14.3 (95% CI, 5.2 to 24.0; \( P_{\text{Cox}} < .0001 \)) and 5.6 (95% CI, 2.0 to 9.3; \( P_{\text{Cox}} = .0012 \)) for radiation-managed patients.

Conclusion: This study provided evidence to support the prediction of time to PCSM after surgery or radiation on the basis of pretreatment risk groups for patients with clinically localized prostate cancer managed during the PSA era.

Radical Prostatectomy-High Risk: 10 year Disease-specific and non-prostate cancer mortality

Fig 4. Prostate cancer— and non-prostate cancer—specific mortality after radical prostatectomy stratified by age at the time of initial therapy and the pretreatment risk group. Blue, prostate cancer—specific mortality; red, non-prostate cancer—specific mortality.
Duke Prostate Center Outcomes Database-
High Risk After Radical Prostatectomy

PSA recurrence free survival

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>PSA Recurrence Free Survival (%)</th>
</tr>
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<tbody>
<tr>
<td>Low</td>
<td>84.9</td>
</tr>
<tr>
<td>Intermediate</td>
<td>71.5</td>
</tr>
<tr>
<td>High</td>
<td>48.1</td>
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</table>

5 year outcome

Log Rank < 0.0001
DPC: Distant metastasis free survival

<table>
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<tr>
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<th>%</th>
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<tr>
<td>Low</td>
<td>99</td>
</tr>
<tr>
<td>Intermediate</td>
<td>98.6</td>
</tr>
<tr>
<td>High</td>
<td>93.1</td>
</tr>
</tbody>
</table>

Log Rank < 0.0001

5 year outcome
DPC: Disease specific death free survival

Log Rank < 0.0001

<table>
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<th>%</th>
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<tbody>
<tr>
<td>Low</td>
<td>0</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0</td>
</tr>
<tr>
<td>High</td>
<td>96.2</td>
</tr>
</tbody>
</table>

5 year outcome

Years after radical prostatectomy
## Evolving Risk Stratification

<table>
<thead>
<tr>
<th>Clinically Localized</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Very low risk</strong></td>
<td>T1c; Gleason score ≤6; PSA &lt;10 ng/mL; Fewer than 3 prostate biopsy cores positive, ≤50% cancer in each core; PSA density &lt;0.15 ng/mL/g</td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td>T1-T2a; Gleason score ≤6; PSA &lt;10 ng/mL</td>
</tr>
<tr>
<td><strong>Intermediate risk</strong></td>
<td>T2b-T2c or Gleason score 7 or PSA 10–20 ng/mL</td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td>T3a or Gleason score 8-10 or PSA &gt;20 ng/mL</td>
</tr>
<tr>
<td><strong>Very high risk</strong></td>
<td>T3b-T4 or Primary Gleason pattern 5 or &gt;4 cores with Gleason score 8-10</td>
</tr>
</tbody>
</table>
Surgical Options for High Risk CAP

- RP alone
- RP with neoadjuvant HT
- RP with adjuvant EBRT and/or HT
- Clinical Trials including RP
Neoadjuvant Hormonal Therapy and RP

- Multiple studies using 3–8 months of NHT
  - 50% reduction in positive margins
  - Up to 50% size reduction
- Conclusions
  - No impact on PSA progression
  - No longer recommended for “downstaging”
  - May have a role in mechanical “downsizing”

High Risk: Neoadjuvant ADT and RP

Recent SWOG 9109 update (10 year f/u)

- N = 61 men with cT3/4 PC, median PSA 20
- 4 mos ADT with CAB (goserelin + flutamide) then RP
- 30% pathologic Gleason grade not interpretable
  - (a good or bad sign)?
- 10 year PFS 40%, OS 68%
- Similar to RT + ADT for high-risk (i.e. EORTC 22863 – 10 year OS 58%)

Berglund, et al. Urology
RP with Adjuvant HT

- Single center data suggest disease control; no survival data
- Best data to support use:
  - ECOG-3886 (Messing) trial
    - HT vs observation in N + RP
    - 7.1 yrs f/u immediate HT better OS (85.1% vs. 64.7%) and DSS (93.6% vs. 68.6%)
  - Bicalutamide EPC trial
    - 2 years bicalutamide 150 mg vs placebo for all RP
    - GS >7 and PSA >10, irrespective of T-stage, has reduced PSA and objective progression based on international experience

Results at 10 Years of EST 3886

Prostate Cancer-specific Survival

Log Rank Test $P < .001$

Post Operative Radiation Therapy

- ADJUVANT
  - Given for positive margins
  - Performed when PSA is still “undetectable” (\( \leq 0.2 \text{ng/ml} \) typically)
  - Recently published positive RCT’s

- SALVAGE
  - Given for a rising PSA ie. Biochemical recurrence
  - No published RCT’s to support use, but very popular
Radiation After Prostate Cancer Surgery Boosts Survival

TUESDAY, OCT. 20 (HealthDay News) -- Men treated with radiation after prostate surgery have a better chance of surviving the disease, compared to those who did not receive adjuvant radiation, researchers report.

That finding was presented Wednesday at the annual meeting of the American Urological Association in Denver.

The study included more than 400 men whose tumors were classified as stage T2b or higher, meaning the cancer was larger than the gland but no bigger than the muscle that surrounds it.

The men who received adjuvant radiation didn't have better survival rates at five years, but after ten years, the study found that nearly 74% of men treated with radiation were still alive, compared to 66% of men who didn't receive this treatment.

"We have known for a long time that men who have had their prostate gland removed are at a decreased risk of dying from prostate cancer," said study co-author Dr. Robert Regan, surgical director of the Southwest Oncology Group, which conducted the trial.

"To see a 25% improvement at 10 years is quite impressive," Regan said.

Prostate cancer is the second most common cancer among men in the United States, and the American Cancer Society estimates that 238,390 men will be diagnosed with prostate cancer in the country this year. About one in six men will get prostate cancer, but the good news is that the rate has been declining;

One reason is earlier diagnosis, according to the cancer society.

More information

The American Cancer Society has more about prostate cancer.
Exploring the Ideal Therapeutic Window for Successful Post-Prostatectomy Salvage Radiotherapy Below a Relapsed PSA of 1.0 ng/mL

Karlin, Hagan, Koontz, Moghanaki, Mukhopadhyay, Moul, Lee, Anscher

Virginia Commonwealth University and Duke University
Methods

• Retrospective database of 317 patients treated for post-prostatectomy PSA failure at VCU and Duke between 1988-2008
  – All patients ruled out for metastasis (bone scan, CT)
  – N+ patients excluded
  – 3D-CRT

• 199/317 treated with pre-RT PSA ≤ 1.0 ng/mL
  – Median follow-up = 5.4 years
# Patient Characteristics

## Clinical Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td>Median age at RP</td>
<td>63 years</td>
<td>(38-75)</td>
</tr>
<tr>
<td>Gleason 8-10</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>+ ECE</td>
<td>46%</td>
<td></td>
</tr>
<tr>
<td>+ SV</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>+ Margins</td>
<td>66%</td>
<td></td>
</tr>
<tr>
<td>Median pre-RP PSA</td>
<td>8.0 ng/mL</td>
<td>(1.8-70)</td>
</tr>
<tr>
<td>Median pre-RT PSA</td>
<td>0.30 ng/mL</td>
<td>(0.07-1.0)</td>
</tr>
<tr>
<td>Median time to SRT</td>
<td>29.8 mo.</td>
<td>(1.6-181)</td>
</tr>
</tbody>
</table>

## Treatment Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median RT dose</td>
<td>66.0 Gy</td>
<td>(60-70.2)</td>
</tr>
<tr>
<td>Adjuvant ADT</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Whole Pelvis RT</td>
<td>46%</td>
<td></td>
</tr>
</tbody>
</table>
Freedom from PSA Failure

Pre-RT PSA ≤ 0.3

Pre-RT PSA 0.31 – 1.0

p = 0.013

Months after SRT
KEY FINDING: PSA x Gleason Interaction

Gleason ≤ 7

(p=0.045)

Gleason 8-10

Pre-RT PSA ≤ 0.3

Pre-RT PSA 0.31 – 1.0

Freedom from PSA Failure

Months after SRT
Radical Prostatectomy/High Risk

- Modern Radical Prostatectomy/ “Not your Father’s Radical Prostatectomy”
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- Patient selection/practical issues
- Open vs. Robotic (RALP)?
Radical Prostatectomy 2017

- RALP has gained in popularity due to perceived minimal invasiveness
- Objective outcomes improvements compared to open RP are difficult to prove
- Skill-set of surgeon is greater driver of outcomes than the type of procedure
- RALP is not cost effective compared to open RP in experienced hands
- Recent randomized trial: no difference
RALP, Open Surgery for PCa Offer Similar Early Results

ROBOTIC-ASSISTED laparoscopic prostatectomy (RALP) results in similar functional outcomes at 12 weeks to open radical retropubic prostatectomy, according to new findings published in *The Lancet*.

For the phase 3 trial, 163 men with clinically localized prostate cancer (aged 35 to 70) from the Royal Brisbane & Women’s Hospital in Queensland, Australia, were randomly assigned to RALP and 163 to open prostatectomy. To minimize heterogeneity, the same surgeon performed all RALPs and another surgeon performed all open procedures from 2010 to 2015. In the 12 weeks after surgery, 131 and 121 men, respectively, completed questionnaires, such as the Expanded Prostate Cancer Index Composite and International Index of Erectile Function.

Results showed that urinary function scores did not differ significantly between groups at 12 weeks after prostatectomy (83.8 vs. 82.5 for open and RALP, respectively),” investigators John W. Yaxley, MBBS, and colleagues reported. Sexual function scores also appeared similar between groups (35.0 vs. 38.9, respectively).

Neither procedure proved superior in the short-term in the proportion of patients with positive surgical margins, according to the investigators.

RALP patients appeared to have better perioperative outcomes, such as shorter operation time, fewer adverse events, less blood loss, fewer complications, and shorter hospital stay. Fourteen patients (9%) in the open surgery group and 6 (4%) in the RALP group had post-operative complications and 8% and 2% of men, respectively, experienced intraoperative adverse events. These outcomes did not translate into an earlier return to work, however.
OPEN vs. RALP in High Risk Disease?

- Does the enhanced visualization (magnification/3-D) of RALP outweigh the lack of tactile ability?
- Does the lower EBL (especially in less experienced surgeons) with RALP justify use?
- How important is tactile with OPEN for high risk?
- Does OPEN tactile improve selective nerve-sparing?
- After neo-adjuvant chemo/EBRT/novel Rx, is safety of surgical approach important?
High Risk Prostate Cancer - Radical Prostatectomy: Take-Home Points

• Radical Prostatectomy is safe and effective for high risk prostate cancer.
• cT3/ Very High-Risk Localized Disease = Multi-Modality Treatment plan critical: RP + adjuvant EBRT +/- ADT
• pT3 after RP: debate between adjuvant vs. salvage EBRT to prostate bed/pelvis.
• No evidence that RALP is superior to OPEN for RP; a RCT in high risk patients should be done.